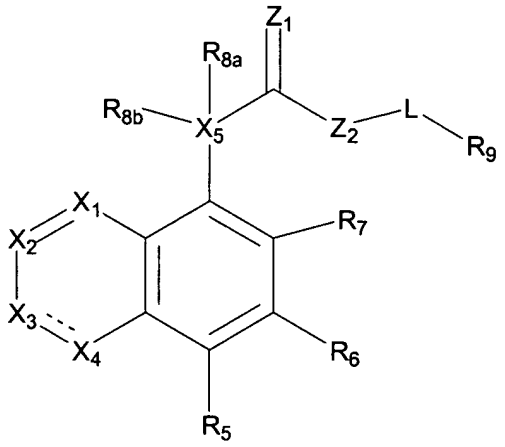
AMENDMENTS TO THE CLAIMS

Claims 1, 77-94 are pending.

The following list of claims will replace prior versions and listing of claims in the application:

1. (Currently Amended) A compound of formula (I)



(I),

or a pharmaceutically acceptable salt or prodrug thereof, wherein

--- is absent or is a single bond;

X_1 is ~~selected from the group consisting of N and~~ CR_1;

X_2 is selected from the group consisting of N and ~~CR_2~~ NR_2;

X_3 is ~~selected from the group consisting of N,~~ NR_3~~, and CR_3~~;

X_4 is a bond; ~~or selected from the group consisting of N and CR_4;~~

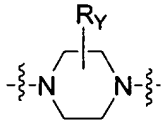
X_5 is ~~selected from the group consisting of~~ N ~~and C~~;

~~provided that at least one of X_1, X_2, X_3, and X_4 is N;~~

Z_1 is ~~selected from the group consisting of O, NH, and S~~;

Z_2 is ~~a bond or selected from the group consisting of~~ NH ~~and O~~;

L is selected from the group consisting of alkenylene, alkylene, alkynylene,



cycloalkylene, , $-(CH_2)_mO(CH_2)_n-$, and $N(R_Y)$, wherein the left end of $-(CH_2)_mO(CH_2)_n-$ is attached to Z_2 and the right end is attached to R_9;

m and n are each independently ~~0~~1-6;

R_Y is selected from the group consisting of hydrogen and alkyl;

R_1, R_3, R_5, R_6, and R_7 are each independently selected from the group consisting of hydrogen, alkenyl, alkoxy, ~~alkoxyalkoxy,~~ alkoxyalkyl, alkoxycarbonyl, alkoxycarbonylalkyl, alkyl, alkylcarbonyl, alkylcarbonylalkyl, alkylcarbonyloxy, ~~alkylthio, alkynyl,~~ carboxy, ~~carboxyalkyl,~~ cyano, cyanoalkyl, cycloalkyl, cycloalkylalkyl, ~~formyl, formylalkyl,~~ haloalkoxy, haloalkyl, haloalkylthio, halogen, hydroxy,

hydroxyalkyl, ~~mercapto, mercaptoalkyl, nitro, $(CF_3)_2(HO)C-$, $-NR_AS(O)_2R_B$,~~ $-S(O)_2OR_A$, $-S(O)_2R_B$, $-NZ_AZ_B$, (NZ_AZ_B)alkyl, (NZ_AZ_B)carbonyl, (NZ_AZ_B)carbonylalkyl and (NZ_AZ_B)sulfonyl, wherein Z_A and Z_B are each independently selected from the group consisting of hydrogen, alkyl, alkylcarbonyl, formyl, aryl, and arylalkyl;

R_2 ~~and R_4 are each~~is independently selected from the group consisting of hydrogen, alkenyl, alkoxy, alkoxyalkoxy, alkoxyalkyl, alkoxycarbonyl, alkoxycarbonylalkyl, alkyl, alkylcarbonyl, alkylcarbonylalkyl, alkylcarbonyloxy, ~~alkylthio, alkynyl,~~ carboxy, carboxyalkyl, cyano, cyanoalkyl, cycloalkyl, cycloalkylalkyl, ~~formyl, formylalkyl,~~ haloalkoxy, haloalkyl, haloalkylthio, halogen, hydroxy, hydroxyalkyl, ~~mercapto, mercaptoalkyl, nitro, $(CF_3)_2(HO)C-$~~, $-NR_AS(O)_2R_B$, $-S(O)_2OR_A$, $-S(O)_2R_B$, $-NZ_AZ_B$, (NZ_AZ_B)alkyl, (NZ_AZ_B)alkylcarbonyl, (NZ_AZ_B)carbonyl, (NZ_AZ_B)carbonylalkyl, and (NZ_AZ_B)sulfonyl, ~~$(NZ_AZ_B)C(=NH)-$, $(NZ_AZ_B)C(=NCN)NH-$, and $(NZ_AZ_B)C(=NH)NH-$~~;

R_A is selected from the group consisting of hydrogen and alkyl;

R_B is selected from the group consisting of alkyl, aryl, and arylalkyl;

R_{8a} is selected from the group consisting of hydrogen and alkyl;

R_{8b} is absent when X_5 is N or R_{8b} is selected from the group consisting of hydrogen, alkoxy, alkoxycarbonylalkyl, alkyl, alkylcarbonyloxy, alkylsulfonyloxy, halogen, and hydroxy when X_5 is C; and

R_9 is selected from the group consisting of hydrogen, aryl, cycloalkyl, and heterocycle.

2-76. (Cancelled)

77. (Currently Amended) The compound according to claim 1 wherein

--- is absent;

~~X_1 is CR_1;~~

X_2 is N;

~~X_3 is NR_3; and~~

~~X_4 is a bond.~~

R_{8b} is absent;

L is alkylene; and

R_9 is aryl.

78. (Cancelled)

79. (Currently Amended) The compound according to claim 77 wherein

~~X_5 is N;~~

R_1, R_5, R_6 and R_7 are each hydrogen; and

~~R_{8b} is absent;~~

~~Z_1 is O;~~

~~Z_2 is NH;~~

~~L is alkylene;~~

R_9 is aryl wherein said aryl is phenyl optionally substituted with 1, 2, or 3 substituents independently selected from the group consisting of alkoxy, alkyl, alkylsulfonyl, 2-azabicyclo[2.2.1]hept-2-yl, 8-azabicyclo[3.2.1]oct-8-yl, 1-azepanyl, 1-azocanyl, cyano, haloalkoxy, haloalkyl, haloalkylthio, halogen, methylenedioxy, 4-morpholinyl, 2,6,-dimethyl-4-morpholinyl, phenyl, 1-piperidinyl, 4-methyl-1-piperidinyl, pyridinyl, 1-pyrrolidinyl, 4-thiomorpholinyl, and $-NZ_CZ_D$; and

Z_C and Z_D are independently selected from the group consisting of hydrogen and alkyl.

80. The compound according to claim 79 selected from the group consisting of
N-(3,4-dichlorobenzyl)-N'-1H-indazol-4-ylurea;
N-1H-indazol-4-yl-N'-[4-(1-piperidinyl)benzyl]urea;
N-[3-fluoro-4-(1-piperidinyl)benzyl]-N'-1H-indazol-4-ylurea;
N-1H-indazol-4-yl-N'-[4-(1-pyrrolidinyl)benzyl]urea;
N-[3-fluoro-4-(1-pyrrolidinyl)benzyl]-N'-1H-indazol-4-ylurea;
N-[4-(1-azepanyl)benzyl]-N'-1H-indazol-4-ylurea;
N-[4-(1-azepanyl)-3-fluorobenzyl]-N'-1H-indazol-4-ylurea;
N-(1-methyl-1H-indazol-4-yl)-N'-[4-(1-piperidinyl)benzyl]urea;
N-[3-fluoro-4-(1-piperidinyl)benzyl]-N'-(1-methyl-1H-indazol-4-yl)urea;
N-(1-methyl-1H-indazol-4-yl)-N'-[4-(1-pyrrolidinyl)benzyl]urea;
N-[3-fluoro-4-(1-pyrrolidinyl)benzyl]-N'-(1-methyl-1H-indazol-4-yl)urea;
N-[4-(1-azepanyl)benzyl]-N'-(1-methyl-1H-indazol-4-yl)urea;
N-[4-(1-azepanyl)-3-fluorobenzyl]-N'-(1-methyl-1H-indazol-4-yl)urea;
methyl 4-({[(1-naphthylmethyl)amino]carbonyl}amino)-1H-indazole-1-carboxylate;
methyl 4-({[(1,1'-biphenyl-3-ylmethyl)amino]carbonyl}amino)-1H-indazole-1-carboxylate;
methyl 4-({[(2-chlorobenzyl)amino]carbonyl}amino)-1H-indazole-1-carboxylate;
methyl 4-[({[2-fluoro-5-(trifluoromethyl)benzyl]amino}carbonyl)amino]-1H-indazole-1-carboxylate;
N-(1,1'-biphenyl-3-ylmethyl)-N'-1H-indazol-4-ylurea;
N-(2-chlorobenzyl)-N'-1H-indazol-4-ylurea;
N-[2-fluoro-5-(trifluoromethyl)benzyl]-N'-1H-indazol-4-ylurea;
N-[2-(2,4-dimethylphenyl)ethyl]-N'-1H-indazol-4-ylurea;
N-[2-(3,4-dichlorophenyl)ethyl]-N'-1H-indazol-4-ylurea;
N-1H-indazol-4-yl-N'-[2-(4-methylphenyl)ethyl]urea;
N-[4-azepan-1-yl-3-(trifluoromethyl)benzyl]-N'-1H-indazol-4-ylurea;
N-[4-azepan-1-yl-2-(trifluoromethyl)benzyl]-N'-1H-indazol-4-ylurea;
N-[4-(2-azabicyclo[2.2.1]hept-2-yl)-2-(trifluoromethyl)benzyl]-N'-1H-indazol-4-ylurea;
N-[4-(8-azabicyclo[3.2.1]oct-8-yl)-2-(trifluoromethyl)benzyl]-N'-1H-indazol-4-ylurea;
N-[4-(8-azabicyclo[3.2.1]oct-8-yl)-3-fluorobenzyl]-N'-1H-indazol-4-ylurea;
N-(3-chloro-4-azepan-1-ylbenzyl)-N'-1H-indazol-4-ylurea;

N-[(1S)-1-(4-bromophenyl)ethyl]-N'-1H-indazol-4-ylurea;
N-(3-bromo-4-fluorobenzyl)-N'-1H-indazol-4-ylurea;
N-(2,4-dimethylbenzyl)-N'-1H-indazol-4-ylurea;
N-(4-chlorobenzyl)-N'-1H-indazol-4-ylurea;
N-[3-fluoro-4-(trifluoromethyl)benzyl]-N'-1H-indazol-4-ylurea;
N-1H-indazol-4-yl-N'-(4-methylbenzyl)urea;
N-1H-indazol-4-yl-N'-[3-(trifluoromethoxy)benzyl]urea;
N-(3-chloro-4-fluorobenzyl)-N'-1H-indazol-4-ylurea;
N-(3,4-dimethylbenzyl)-N'-1H-indazol-4-ylurea;
N-[3-fluoro-5-(trifluoromethyl)benzyl]-N'-1H-indazol-4-ylurea;
N-(2-chloro-4-azepan-1-ylbenzyl)-N'-1H-indazol-4-ylurea;
N-(2,3-dichlorobenzyl)-N'-1H-indazol-4-ylurea;
N-1H-indazol-4-yl-N'-{4-[(trifluoromethyl)thio]benzyl}urea;
N-1H-indazol-4-yl-N'-[3-(trifluoromethyl)benzyl]urea;
N-(3,5-difluoro-4-azepan-1-ylbenzyl)-N'-1H-indazol-4-ylurea;
N-[4-(8-azabicyclo[3.2.1]oct-8-yl)-3,5-difluorobenzyl]-N'-1H-indazol-4-ylurea;
N-(4-chlorobenzyl)-N'-(1-methyl-1H-indazol-4-yl)urea;
N-[4-(8-azabicyclo[3.2.1]oct-8-yl)-2-chlorobenzyl]-N'-1H-indazol-4-ylurea;
methyl 4-[({[4-(8-azabicyclo[3.2.1]oct-8-yl)-3-(trifluoromethyl)benzyl]amino}carbonyl)amino]-1H-indazole-1-carboxylate;
N-[4-(8-azabicyclo[3.2.1]oct-8-yl)-3-chlorobenzyl]-N'-1H-indazol-4-ylurea;
N-[4-(8-azabicyclo[3.2.1]oct-8-yl)benzyl]-N'-1H-indazol-4-ylurea;
N-(4-tert-butylbenzyl)-N'-(1-methyl-1H-indazol-4-yl)urea;
N-[3-fluoro-4-(trifluoromethyl)benzyl]-N'-(1-methyl-1H-indazol-4-yl)urea;
N-[4-chloro-3-(trifluoromethyl)benzyl]-N'-(1-methyl-1H-indazol-4-yl)urea;
N-(3,4-dichlorobenzyl)-N'-(1-methyl-1H-indazol-4-yl)urea;
N-(2,4-dichlorobenzyl)-N'-(1-methyl-1H-indazol-4-yl)urea;
N-(4-ethylbenzyl)-N'-(1-methyl-1H-indazol-4-yl)urea;
N-(2-chlorobenzyl)-N'-(1-methyl-1H-indazol-4-yl)urea;
N-(4-fluorobenzyl)-N'-(1-methyl-1H-indazol-4-yl)urea;
N-(2-fluorobenzyl)-N'-(1-methyl-1H-indazol-4-yl)urea;
N-[1-(4-bromophenyl)ethyl]-N'-(1-methyl-1H-indazol-4-yl)urea; and
N-(1-methyl-1H-indazol-4-yl)-N'-{4-[(trifluoromethyl)thio]benzyl}urea.

81. (Currently Amended) The compound according to claim 77 wherein
R_{8a}, R_1, R_5, R_6 and R_7 are each hydrogen;
~~R_{8b} is absent;~~
~~X_5 is N;~~
~~Z_1 is O;~~
~~Z_2 is NH;~~
L is alkylene wherein the alkylene is $-CH_2-$;
R_9 is aryl wherein said aryl is phenyl substituted with 2 substituents independently selected from the group consisting of (8-azabicyclo[3.2.1]oct-8-yl), trifluoromethyl, and -Cl;

and
R_3 is selected from the group consisting of hydrogen and alkoxycarbonyl.

82. (Currently Amended) The compound according to claim 77 wherein
R_{8a}, R_1, R_5, R_6 and R_7 are each hydrogen;
~~R_{8b} is absent;~~
~~X_5 is N;~~
~~Z_1 is O;~~
~~Z_2 is NH;~~
L is alkylene wherein the alkylene is $-CH_2-$;
R_9 is aryl wherein said aryl is 4-(8-azabicyclo[3.2.1]oct-8-yl)-3-(trifluoromethyl)phenyl; and
R_3 is selected from the group consisting of hydrogen and alkoxycarbonyl.

83. (Currently Amended) The compound according to claim 77 wherein
R_{8a}, R_1, R_5, R_6 and R_7 are each hydrogen;
~~R_{8b} is absent;~~
~~X_5 is N;~~
~~Z_1 is O;~~
~~Z_2 is NH;~~
L is alkylene wherein the alkylene is $-CH_2-$;
R_9 is aryl wherein said aryl is 2-chloro-4-(8-azabicyclo[3.2.1]oct-8-yl)phenyl; and
R_3 is selected from the group consisting of hydrogen and alkoxycarbonyl.

84. The compound according to claim 81 selected from the group consisting of
N-[4-(8-azabicyclo[3.2.1]oct-8-yl)-2-chlorobenzyl]-N'-1H-indazol-4-ylurea; and
N-[4-(8-azabicyclo[3.2.1]oct-8-yl)-3-(trifluoromethyl)benzyl]-N'-1H-indazol-4-ylurea.

85. (Currently Amended) The compound according to claim 77 wherein
~~X_5 is N;~~
R_1, R_6 and R_7 are each hydrogen;
R_5 is alkyl; and
~~R_{8b} is absent;~~
~~Z_1 is O;~~
~~Z_2 is NH;~~
~~L is alkylene;~~
R_9 is aryl wherein said aryl is phenyl optionally substituted with 1, 2, or 3 substituents independently selected from the group consisting of alkoxy, alkyl, alkylsulfonyl, 2-azabicyclo[2.2.1]hept-2-yl, 8-azabicyclo[3.2.1]oct-8-yl, 1-azepanyl, 1-azocanyl, cyano, haloalkoxy, haloalkyl, haloalkylthio, halogen, methylenedioxy, 4-morpholinyl, 2,6,-dimethyl-4-morpholinyl, phenyl, 1-piperidinyl, 4-methyl-1-piperidinyl, pyridinyl, 1-pyrrolidinyl, 4-thiomorpholinyl, and $-NZ_CZ_D$; and

Z_C and Z_D are independently selected from the group consisting of hydrogen and alkyl.

86. The compound according to claim 85 selected from the group consisting of
N-(4-tert-butylbenzyl)-N'-(7-methyl-1H-indazol-4-yl)urea;
N-(7-methyl-1H-indazol-4-yl)-N'-[4-(trifluoromethyl)benzyl]urea; and
N-(7-methyl-1H-indazol-4-yl)-N'-{4-[(trifluoromethyl)thio]benzyl}urea.

87. (Currently Amended) The compound according to claim 77 wherein
~~X_5 is N;~~
R_1, R_5, R_6 and R_7 are each hydrogen;
~~R_5 is alkyl;~~
~~R_{8b} is absent;~~
~~Z_1 is O;~~
~~Z_2 is NH;~~
~~L is alkylene; and~~
R_9 is aryl wherein said aryl is selected from the group consisting of naphthyl and phenyl.

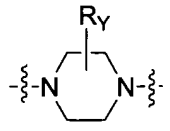
88. The compound according to claim 87 selected from the group consisting of
N-1H-indazol-4-yl-N'-(1-naphthylmethyl)urea; and
N-1H-indazol-4-yl-N'-(3-phenylpropyl)urea.

89. (Currently Amended) The compound according to claim 77 wherein
~~X_5 is N;~~
R_1, R_5, R_6 and R_7 are each hydrogen; and
~~R_{8b} is absent;~~
~~Z_1 is O;~~
~~Z_2 is NH;~~
~~L is alkylene; and~~
R_9 is heterocycle wherein said heterocycle is pyridinyl optionally substituted with 1 or 2 substituents independently selected from the group consisting of alkoxy, alkyl, alkylsulfonyl, 2-azabicyclo[2.2.1]hept-2-yl, 8-azabicyclo[3.2.1]oct-8-yl, 1-azepanyl, 1-azocanyl, cyano, haloalkoxy, haloalkyl, haloalkylthio, halogen, methylenedioxy, 4-morpholinyl, 2,6,-dimethyl-4-morpholinyl, phenyl, 1-piperidinyl, 4-methyl-1-piperidinyl, pyridinyl, 1-pyrrolidinyl, 4-thiomorpholinyl, and $-NZ_CZ_D$.

90. The compound according to claim 89 that is N-1H-indazol-4-yl-N'-{[6-(trifluoromethyl)-3-pyridinyl]methyl}urea.

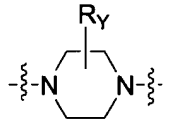
91. (Currently Amended) The compound according to claim 77 wherein
~~X_5 is N;~~
~~R_{8b} is absent;~~
~~Z_1 is O;~~

~~Z_2 is NH;~~
L is



; and
R_9 is heterocycle.

92. (Currently Amended) The compound according to claim 77 wherein
~~X_5 is N;~~
R_1, R_5, R_6 and R_7 are each hydrogen;
~~R_{8b} is absent;~~
~~Z_1 is O;~~
~~Z_2 is NH;~~
L is



;
R_9 is heterocycle wherein said heterocycle is pyridinyl optionally substituted with 1 or 2 substituents independently selected from the group consisting of alkoxy, alkyl, alkylsulfonyl, 2-azabicyclo[2.2.1]hept-2-yl, 8-azabicyclo[3.2.1]oct-8-yl, 1-azepanyl, 1-azocanyl, cyano, haloalkoxy, haloalkyl, haloalkylthio, halogen, methylenedioxy, 4-morpholinyl, 2,6,-dimethyl-4-morpholinyl, phenyl, 1-piperidinyl, 4-methyl-1-piperidinyl, pyridinyl, 1-pyrrolidinyl, 4-thiomorpholinyl, and $-NZ_CZ_D$; and
Z_C and Z_D are independently selected from the group consisting of hydrogen and alkyl.

93. (Currently Amended) ~~A~~The compound according to claim 92 that is N-(1-methyl-1H-indazol-4-yl)-4-[4-(trifluoromethyl)-2-pyridinyl]-1-piperazinecarboxamide.

94. (Currently Amended) A pharmaceutical composition comprising a therapeutically effective amount of a compound of formula (I) as defined in claim 1, or a pharmaceutically acceptable salt thereof.

95. (Currently Amended) A method of treating a disorder wherein the disorder is ameliorated by inhibiting vanilloid receptor subtype 1 (VR1) receptor, and wherein the disorder is selected from the group comprising pain, bladder overactivity, urinary incontinence and inflammatory thermal hyperalgesia in a host mammal in need of such treatment comprising administering a therapeutically effective amount of a compound of formula (I) as defined in claim 1, or a pharmaceutically acceptable salt thereof.

96. (Currently Amended) A method of treating bladder overactivity in a host mammal in need of such treatment comprising administering a therapeutically effective amount of

a compound of formula (I) as defined in claim 1, or a pharmaceutically acceptable salt thereof.

97. (Currently Amended) A method of treating urinary incontinence in a host mammal in need of such treatment comprising administering a therapeutically effective amount of a compound of formula (I) as defined in claim 1, or a pharmaceutically acceptable salt thereof.

98. (New) A method of treating pain in a host mammal in need of such treatment comprising administering a therapeutically effective amount of a compound of formula (I) as defined in claim 1, or a pharmaceutically acceptable salt thereof.

99. (New) A method of treating inflammatory thermal hyperalgesia in a host mammal in need of such treatment comprising administering a therapeutically effective amount of a compound of formula (I) as defined in claim 1, or a pharmaceutically acceptable salt thereof.